The Impact of Exposure Classification Strategies and Water Consumption Information on Exposure Estimates of Water-Borne Contaminants

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◀Background

- Disinfection by-products (DBPs) have been associated with various reproductive and developmental outcomes (e.g. low birth weight, stillbirths), mostly based on indirect exposure assessment methods (e.g., town average concentrations) which assume equal exposure levels for all residents
- DBP Exposure Assessment limitations (including unknown variability in individual water use patterns and spatial/temporal variability in DBP formation) can result in Exposure Misclassification which can Bias study findings and reduce statistical power to detect associations

◀Objectives

- Through a cooperative agreement, an international collaborative effort with scientists from the U.S. Environmental Protection Agency (U.S. EPA) and universities in the United States and the United Kingdom was established to refine exposure assessment methods for a prospective epidemiologic study of spontaneous abortions and DBP exposure
- Computer simulations of drinking water distribution system average concentrations were used to examine the impact of water behavior modifying factors (i.e. water intake including bottled and filtered water use) on exposure misclassification
- The magnitude of exposure misclassification from the use of system average concentrations was quantified using four categorization strategies determined from DBP percentile distributions

◀Methods

Modeling Assumptions & Simulation Sampling Strategy (n=1000 Iterations)

- 100 subjects were equally distributed across 10 different service areas
- Each water system had different average DBP concentrations (range 0-99 µg/L) with system concentrations increasing by 10 µg/L per service area designation
- Limited intra-system variability existed among subjects residing in the same town (i.e., exposures were within 9 µg/L)
- 20% of subjects were exclusive bottled water users
- Bottled water contained no DBPs
- 20% of subjects were exclusive filtered water users
- 50% or 90% of DBPs were removed following point-of-use filtration of home tap water
- Water intake levels (with percent of subjects) included: 0.5 L/day (10% of subjects); 1.0 L/day (30% of subjects); 1.5 L/day (30% of subjects); 2.0 L/day (20% of subjects); 2.5 L/day (10% of subjects)
- Ingestion was the primary exposure route of interest (e.g., non-volatile DBPs)
- Hot water intake was similar across all subjects, and any changes in DBP concentration upon heating or boiling were reflected in the average DBP concentrations
- Tap water exposures occurring outside the home were similar among the subjects

◀Misclassification Approach

Subjects were classified into low, intermediate, high, and very high exposure groups based on the system average concentration percentiles. Following incorporation of the exposure modifying data, individual exposure scores were re-calculated. Subjects were re-classified into exposure groups and compared to system average classifications. Misclassification across one exposure group (e.g., from low to intermediate) or across at least two exposure groups (e.g., from high to low) was calculated.

◀Exposure Categories

Trichotomous Approaches
- Median (50%, 40%, 10%)
- Tertile (34%, 33%, 33%)
- 40th percentile (40%, 30%, 30%)

Four Category Approach
- 40th percentile (40%, 30%, 20%, 10%)

◀Average DBP Intake (AI) Formula

AI = DBP level (0-99 µg/L) *x* Water Intake (0.5-2.5 L/day) *x* Bottled or filtered water modification (0, 50% or 90%)

e.g., Subject #1: Exclusive Filtered Water User (1.0 L/day) with 50% removal & Mean DBP concentration=80 µg/L

AI = 80 µg/L *x* 1.0 L/day *x* 0.5= 40 µg/day

DBP concentration (80 µg/L) → Consumption rate (1.0 L/day) → Filter use with 50% filtration efficiency

Trichotomous Exposure Category (based on system avg. DBP level)	Trichotomous Exposure Category (based on avg. DBP & consumption)	Trichotomous Exposure Category (based on avg. DBP, cons. & 50% removal)
Low	Low	Low
Intermediate	Intermediate	Intermediate X
High X	High X	High

◀Results

- Mean and median DBP exposure was 50 µg/L based on town average concentrations
- Mean water consumption was 1.45 L/day
- Correlations (r) between different exposures ranged from 0.66-0.91 for system average concentrations relative to scores based on one exposure modifier, but were less correlated when more than one exposure modifier was considered (r=0.49-0.76)
- Relative to exposure estimates using individual water use data, average misclassification ranged from 30-51% and 38-62% following incorporation of 2 and 3 exposure modifying factors, respectively (Table 1)
- Most of the misclassification (36-47%) was within one exposure category, although up to 14% of subjects were misclassified across at least two exposure groups (Table 2)
- The Median approach resulted in the least misclassification and the Four Category approach resulted in the most misclassification (Tables 1 & 2)

TABLE 1. Percentage of subjects misclassified compared to original system average exposure category

	DBP Intake Modified for Exclusive Filtered Water or Bottled Water (BW) Use			DBP Intake Modified for Exclusive Filtered Water or Bottled Water (BW) Use	
Exposure Classification Strategy	Intake & 50% Filter	Intake & 90% Filter	Intake & BW	Intake & BW & 50% Filter	Intake & BW & 90% Filter
50-40-10%[a]	30	36	36	38	48
34-33-33%[b]	34	43	43	45	55
40-30-30%[c]	35	43	43	44	54
40-30-20-10%[d]	44	51	51	51	62

TABLE 2. Percentage of subjects misclassified across at least two exposure categories compared to original system average exposure category

	DBP Intake Modified for Exclusive Filtered Water or Bottled Water (BW) Use			DBP Intake Modified for Exclusive Filtered Water or Bottled Water (BW) Use	
Exposure Classification Strategy	Intake & 50% Filter	Intake & 90% Filter	Intake & BW	Intake & BW & 50% Filter	Intake & BW & 90% Filter
50-40-10%[a]	1	2	2	2	4
34-33-33%[b]	1	6	7	7	9
40-30-30%[c]	3	6	7	8	10
40-30-20-10%[d]	6	9	9	11	14

[a] ≤ 50th percentile comprised the low exposure group; between the 50th and 90th percentile comprised the intermediate exposure group; ≥ 90th percentile comprised the high exposure group.
[b] ≤ 34th percentile comprised the low exposure group; between the 34th and 68th percentile comprised the intermediate exposure group; ≥ 68th percentile comprised the high exposure group.
[c] ≤ 40th percentile comprised the low exposure group; between the 40th and 70th percentile comprised the intermediate exposure group; ≥ 70th percentile comprised the high exposure group.
[d] ≤ 40th percentile comprised the low exposure group; between the 40th and 70th percentile comprised the intermediate exposure group; between the 70th and 90th percentile comprised the high exposure group; ≥ 90th percentile comprised the very high exposure group.

◀Discussion

- Water intake level (L/day) was the most influential exposure modifying factor since it impacted exposure scores for all of the subjects (versus 20% of subjects with filtered & bottled water use)
- Minimal differences in misclassification were observed for an assumption of 50% versus 90% DBP removal efficiency among exclusive filtered water users
- Two of the exposure modifiers (filtered and bottled water use) resulted in lower exposures, therefore categorical approaches that had more subjects in the low group (e.g., Median approach) were subject to less misclassification
- The Median approach resulted in less extreme misclassification (across at least two categories), since a smaller fraction of the population (i.e., low and high groups) were able to be misclassified across at least two exposure groups
- The Four Category approach resulted in the most extreme misclassification (up to 14%) since all of the subjects could be misclassified across two categories
- Despite relatively high correlations with more direct measurements, considerable misclassification was detected following the use of system average concentrations
- The impact of exposure misclassification on existing epidemiologic findings is unknown, but Reif et al. (2000) showed that 20% non-differential misclassification of low exposures into intermediate and high exposure groups resulted in considerable bias towards the null

◀Conclusions

- These data highlight the importance of collecting detailed individual-level information to improve exposure characterization and accurately quantify DBP exposure misclassification bias in epidemiologic studies
- These findings address some of the uncertainties in existing studies due to exposure misclassification from use of town average concentrations – a critical need for DBP regulatory rule-making

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